REMARKS

Claims 6 and 8 have been cancelled.

Claims 1-3, 5 and 13 have been amended.

New Claim 23 has been added.

Claims 1- 8 and 13 are under examination.

Reconsideration is respectfully requested in view of the above amendment and the following remarks.

Rejection under 35 USC 102(a)

The Examiner rejects claims 1, 3, 5-8 and 13 under 35 USC 102(a) as being anticipated by Brown and Bertelli (March 22, 2001, WO 01/19870 A2), because Brown and Bertelli teach a nucleic acid molecule encoding a polypeptide that is 97.5% identical to polypeptide of SEQ ID NO:10 in the present application.

Applicants hereby submit a declaration together with copies of the relevant notebook pages and the computer printout under Rule 37 CFR 1.131 to demonstrate that the present invention had completed prior to March 22, 2001, the publication date of the Brown and Bertelli publication.

Applicants respectfully submit that Brown and Bertelli is not a prior art to the present invention under 35 USC 102(a), since the present invention predates Brown and Bertelli publication. Accordingly, the rejection under 35 USC 102(a) over Brown and Bertelli has been overcome and should be withdrawn.

Rejection under 35 USC 103(a)

The Examiner rejects claim 2 under 35 USC 103(a) as being obvious over Brown and Bertelli in view of Klugbauer et al. (1999, Journal of Neurosecience).

Brown and Bertelli has been removed as a prior art reference under 35 USC 102(a) in connection with the discussion on the 35 USC 102(a) rejection above. Absent Brown and Bertelli, there would be no sufficient basis for a rejection under 35 USC 103(a). Accordingly, applicants respectfully submit that the rejection under 35 USC 103(a) has been overcome and should be withdrawn.

Rejection under 35 USC 112, first paragraph

The Examiner rejects claims 103, 5-8 and 13 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner stated that "[the] claims are drawn to isolated nucleic acids encoding polypeptides having at least a 95% to a polypeptide comprising amino acids 1 to 1090 of SEQ ID NO: 10, and variants and fragments thereof"; and that "[the] claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature." "Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity or hybridization ability."

Applicants have amended claims as shown above. The claims now are directed to an isolated nucleic acid molecule encoding a polypeptide having a sequence and biological activities substantially same as a polypeptide of SEQ ID NO: 10. Amended claims are now limited to include only insubstantial changes of SEQ ID NO: 10, as such insubstantial changes can be made by routine experimentation. This amendment is supported by the specification (See pages 28-19).

In view of the amendment, applicants respectfully submit that the rejection under 35 USC 112, first paragraph, has been overcome and should be withdrawn.

Rejection under 35 USC 112, second paragraph

The Examiner rejects claims 1-3 and 13 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner believes that the claim terms "hybridizes under stringent conditions" in claim 1(d), "the nucleic acid molecule of claim 1" in claims 2 and 3, "transferring" an expression vector in claim 13(a) are indefinite.

With respect to "stringent conditions" in claim 1(d), the specification provides a detailed the description and examples on pages 30-31.

With respect to "the nucleic acid ..." in claims 2 and 3, applicants have amended it to read "any of the nucleic acid molecules in claim 1".

With respect to the word "transferring" in claim 13(a), applicants have changed it to "introducing" and the support and definition of "introducing" can be found on page 36.

In view of the amendment to the claim language and the supports in the specification, applicants respectfully submit that rejection under 35 USC 112, second paragraph, has been overcome and should be withdrawn.

Rejection under 35 USC 101 and 112, first paragraph

The Examiner rejects claims 1-8 and 13 under 35 USC 101 and 112, first paragraph on the ground that the claimed invention is not supported by either a credible, substantial or specific asserted utility or a well established utility. Applicants respectfully disagree with the Examiner's conclusion.

The present invention is directed to a gene encoding a subunit or component of the well documented voltage-gated calcium channel. It has been well established that voltage-gated calcium channels are important mediators of several physiological processes, including neuronal excitability and muscle contraction. Study of voltage-gated calcium channels is a basis for discovery of new therapeutic drugs that is involved in pain management as well as treatments of other physiological conditions.

The voltage-gated calcium channel is composed of a pore-forming α1 subunit and several regulatory subunits: α2δ, β, and γ. α2δ-4 belongs to the α2δ family, which regulates Ca^{2+} influx. It has been demonstrated that α2δ-4 subunit significantly increases calcium influx mediated by CaV1.2/β3 channel in HEK293 cells. N. Qin, *et al*, 2002, *Mol. Pharm.* 62: 485-496. Because of the importance of the voltage-gated calcium channel in the human body, each of the subunit of the voltage-gated calcium channel has been extensively studied and the results of the studies has been reported in numerous scientific journals. Apparently, simply being a component of the voltage-gated calcium channel is sufficient to satisfy the utility requirement, as changes of the calcium channel, which result from the changes of each individual subunit, would result in significant physiological consequences. Thus, discovery and cloning of α2δ-4 subunit has a real world utility, whether such utility is apparent or inherent at the present. At minimum, it is a useful research tool which can lead to a better understanding of the mechanism of the calcium channel and to the discovery of new therapeutic drugs, e.g. for pain management. The fact that other scientists, for example, Brown and Bertelli (See WO 01/19870), have also focused on the study of α2δ-4 subunit supports the notion that α2δ-4 subunit is physiologically significant.

While it is undisputable that the α2δ-4 subunit is physiologically significant and the significance of cloning of α2δ-4 gene is far beyond merely useful, the mechanism how α2δ-4 subunit regulates calcium influx is less understood as compared with other calcium channel subunits, because α2δ-4 gene cloning was a relatively new event. That is precisely why cloning of α2δ-4 subunit marks an important step in the advancement of the study on the voltage-gated calcium channel. Since the α2δ-4 subunit was cloned, more information regarding the mechanism how α2δ-4 subunit works has been generated. N. Qin, *et al.*, *id.* Without the cloned α2δ-4 subunit gene, there would be no understanding at all about the α2δ-4' function and the understanding of the voltage-gated calcium channel would be incomplete.

Applicants respectfully submit that the Examiner erred in concluding that there is no credible utility with respect to α2δ-4 subunit, because the utility of α2δ-4 subunit has been recognized by persons of ordinary skill in the art although its precise mode of action is still a subject of the ongoing research. It is one thing to patent a nucleic acid sequence that no one knows what it is for, but quite another to procure a patent on an identified physiologically significant gene. The lack of knowledge how this gene functions cannot be the basis to negate its utility.

Further more, there is no requirement in the patent law that applicants must know the mechanism of their invention to establish that the invention is useful. By requiring applicants to state the mechanism of α2δ-4 subunit, the Examiner has applied an undue restriction to the patentable subject matter under 35 USC 101 and 112.

Thus, applicants respectfully request that rejection under 35 USC 101 and 112 be withdrawn.

Objection to the specification

The Examiner objects the specification for lacking the sequence identifiers for the sequences disclosed on page 62, lines 8, 9, 13, 14 and 23, page 63, line 23 bridging page 64, lines 1 and 2 and pages 66-69. Applicants have reviewed these portions of the specification according to the Examiner's direction and respectfully submit that the indicated sequences are properly identified with the sequence identifiers. No amendment needs to be made.

In view of the above amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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